REMARKS

In the Office Action mailed May 2, 2007, Claims 35, 48-52, 54-61, 65, and 72-82 are pending for consideration. All of the claims were objected to and rejected on various statutory grounds, each of which is addressed in turn below.

By the present amendment, Claims 35 and 60 have been amended to correct minor grammatical errors pointed out by the Examiner. Additionally, claims 35, 59, and 60 has been amended to provide additional clarity with respect to the terms "caprylic acid more/diglycerides and mono- and diacetylated monoglycerides." Claims 35, 59, and 60 has also been amended to limit the release modulators of the claim. Support for the amendments can be found in the published specification in paragraphs [0062] to [0065]. Additionally, claims 35, 59, and 60 have been amended to include the limitation that at least 95wt% the cilostazol in the formulation is present in a suspended form. Support for this amendment is inherently found in Example 2. The accompanying declaration under 37 C.F.R. § 1.132 by Chandrashekar Giliyar provides additional support for amendment. Claims 35, 59, and 60 were also amended to include the limitation in which the cilostazol is released over an extended period of time. Support for that amendment can be found in originally filed claim 47. Claims 48 and 72 have been amended to correct their dependency. Claims 42-47 and claims 66-71 have been canceled. Applicants submit that no new matter has been added in the by the above described amendments.

It is to be understood that all amendments have been made solely for the purpose of expediting prosecution of the present application, and without conceding the correctness of the Examiner's rejection. Accordingly, Claims 35, 48-52, 54-61, 65, and 72-82 are pending for consideration in the present application. Applicants respectfully submit that the present claims are allowable over the cited references, and that the rejections in view thereof are now moot.

Claim Objections

The Examiner objected to claims 35 and 60 for having minor grammatical errors. The errors cited the Examiner have been amended as shown set forth above.

35 U.S.C. 112 Rejections:

First Paragraph

Claims 35, 47-52, 59, and 72-74 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement with respect to the phrase "a release modulator which synchronizes the release of the drug and the solubilizer." As described above, the Applicants have amended Claim 35 to include specific lists of release modulators which can used to accomplish the present invention. Applicants assert that the present amendment of claim 35 provides ample written description as required under 35 U.S.C. §112, first paragraph, and respectfully request that this rejection be withdrawn.

Claims 42-44, 46, 66-68, and 70 were each rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement. In view of the amendment to claims 35 and 60, each of the rejected claims has been canceled. As such this rejection is moot.

Second Paragraph

Claims 35, 42-52, 59-61, 65-76, and 82 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Specifically, the Examiner rejected claims 35, 59, and 60 for allegedly lacking clarity with respect to the phrase "capryllic acid mono/diglycerides and mono- and diacetylated monoglycerides." Additionally, the Examiner has rejected claim 35 for the use

of the phrase "200-8000 MW". Applicants have amended claims 35, 59, and 60 as described above in order to enhance the clarity of claim the claims. As such, the Applicants request that the Examiner to withdraw the rejection.

The Examiner also rejected claims 42-43, 45, 66-67, and 69 under 35 U.S.C. 112, second paragraph as allegedly being indefinite with respect to the phrase "racemers, enantiomers, or mixtures thereof. As each of the rejected claims has been canceled, this rejection is moot.

The Examiner also rejected claims 72-74 under 35 U.S.C. 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Claim dependency of claim 72 has been amended in order to overcome this rejection. As such, Applicants request that the rejection be withdrawn.

Obviousness-Type Double Patenting Rejections:

The Examiner has provisionally rejected presently pending claims 35, 42-52, and 54-61 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the composition claims of copending U.S. Patent Applications Nos. 10/764,016; and 11/122,788. Applicants submit herewith terminal disclaimers with respect to the cited references. As such, Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. § 103 Rejections:

The Examiner has rejected Claims 35, 42-52, 54-56, 59-61, 65-69, 75-79, and 82 under 35 U.S.C. § 103(a) as being allegedly unpatentable over the U.S. Patent No. 5,891,469 to Amselem et al. (hereinafter "Amselem") patent in view of The Merck Index (Eleventh Edition, Monograph 2277, 1989; pages 353-354). Applicants have amended each of claims 35, 59, and

60 to include a limitation the limitation that the cilostazol be released over an extended period of time." Amselem teachces a solid dry coprecipitate of lipophilic active ingredients and tocopherol polyethyleneglycol succinate (TPGS) which is formed when the active ingredient is co-melted with the TPGS. The coporecipitates can be incorporated into oral dosage forms to provide improved release of the active agent in vitro and enhanced oral bioavailability. However, Amselem does not teach delivering cilostazol, or any other active agent, over an extended period of time. In fact, all of the release profiles taught by Amselem show immediate release of the active agents. As such, Amselem fails to teach each and every element of the pending claims. Therefore, Applicants respectfully request that the present rejection be withdrawn.

The Examiner has also rejected claims 35-42-52, 57-61, 66-76, and 80-82 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,342,625 to Hauer et al (hereinafter "Hauer") in view of all or some of The Merck Index (Eleventh Edition, Monograph 2277, 1989; pages 353-354), U.S. Patent No. 5,891,845 to Myers et al (hereinafter "Myers"), U.S. Patent No. 6,458,373 to Lambert et al (hereinafter "Lambert") and U.S. Patent No. 5,403,593 to Royce (hereinafter "Royce").

Hauer teaches pharmaceutical compositions for delivering cyclosporine in microemulsion form having a hydrophilic phase, a lipophilic phase and a surfactant (Col. 6, lns. 45-53). The cyclosporine is found or carried in the lipophilic phase. Hauer teaches that a disadvantage of previous cyclosporine delivery compositions is that there was a tendency to form cyclosporine precipitate (Col. 3, lns. 40-56). In other words Hauer teaches away from delivery formulations which have solid or precipitated active agent. Further, the microemulsions taught in Hauer are said to "exhibit thermodynamic stability, that is they will remain stable at ambient temperatures, e.g. without clouding or regular emulsion size droplet formation or precipitation, over prolonged

periods of time" (Col. 6, ln.63 to Col. 7, ln. 1). In other words, the active agent in the Hauer compositions is solubilized in the lipophilic phase of the micro-emulsion formulation so that it does not precipitate out. As such, Hauer does not teach having at least 95 wt% of the active agent suspended in the composition as required by the presently amended claims. Additionally, as conceded by the Examiner in the office action (page 17, 1st paragraph), Hauer does not teach the release of the active agent over an extended period of time," (emphasis added) as required by the presently amended claims.

The secondary reference, Myers, relied upon by the Examiner to teach "the advantages of controlled release formulations to improve therapeutic value of the active drug component" teaches Vitamin E TPGS/drug compositions and related methods. The active agent in the compositions is said to be "dissolved directly into Vitamin E TPGS to form a true molecular solution—not an emulsion or micro-emulsion." (emphasis added) It is noteworthy that Myers does not teach a formulation is which at least 95 wt% of the active agent is suspended in the composition as required by the pending claims.

In characterizing the prior art, Myers states the following:

> "The emulsion and micro-emulsion cyclosporine formulations of the prior art suffer numerous disadvantages. They employ highly complex systems that provide generally immediate release formulation that disperse quickly in gastrointestinal tract, thereby permitting the amount of dissolved cyclosporine to be rapidly absorbed and taken into the blood stream at once." (Col. 8, lns. 44-50) (emphasis added)

In addition to the negative characterization of emulsion and micro-emulsion formulations and their numerous disadvantages, Myers specifically negatively characterizes and distinguishes Hauer as being "overly complex" and "seek[ing] to achieve immediate release and absorption of the drug." (Col. 8, ln. 56 to Col. ln. 16). Myers further states that Hauer's "[m]icroemulsions are dispersed quickly out of the emulsion into small particles that will be absorbed in the gut

fairly quickly, if not instantly," (Col. 10, lines. 64-67)(emphasis added). Myers also distinguishes itself from Hauer and other emulsion and micro-emulsion formulations stating that "[t]he solid TPGS /drug composition of the present invention does not require the use of surfactants or non-evaporated co-solvents...In addition, the new drug TPGS/drug delivery system of the present invention provides a slowly dissolving matrix ..." (Col. 11, lns.4-15) (emphasis added). In other words, Myers clearly distinguishes and teaches away from the compositions of Hauer and other emulsion and micro-emulsion formulations.

As the Applicant has raised the issue of teaching away, the Applicant would like to review the current case law regarding teaching away for the Examiner's convenience. The Court of Appeals for the Federal Circuit has clearly stated that "an applicant may rebut a prima facie case of obviousness by showing that the prior art teaches away from the claimed invention in any material respect." In re Petersen, 315 F.3d 1325, 1331 (Fed. Cir. 2003). The Court has also stated that "[w]e have noted elsewhere, as a 'useful general rule,' that references that teach away cannot serve to create a prima facie case of obviousness." (emphasis added) McGinley v. Franklin Sports, Inc., 262 F.3d 1339, 1354 (Fed. Cir. 2001). In identifying the appropriate standard for teaching away, the Court has further stated:

> "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be **discouraged from following the path set out in the reference**, or would be led in a direction divergent from the path that was taken by the applicant. The degree of teaching away will of course depend on the particular facts; in general, **a reference will teach away if it suggests** that the **line of development** flowing from the reference's disclosure **is unlikely to be productive** of the result sought by the applicant." (emphasis added) In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994).

Clearly in the present case, a person of ordinary skill in the art would be discouraged from utilizing the teachings of Myers, which expressly references Hauer and other cyclosporine

micro-emulsion formulations as "suffer[ing] numerous disadvantages," including being "overly complex," and releasing the drug "fairly quickly, if not instantly." Certainly, one skilled in the art would recognize the present combination of references as being contradictory to Myers teachings and thereby "unlikely to be productive of the result sought by the applicant."

Accordingly, the Applicant's respectfully submit that neither Hauer nor Myers teaches or suggests each and every element of the present invention, either alone, in combination, or in any other otherwise modified with Lambert or Royce as suggested by the Examiner. Moreover, Applicants submit that the combination of Hauer and Myers together is improper as Myers clearly teaches away from such a combination. Therefore, Applicants submit that the rejection of the present claims using Hauer and Myers is improper and respectfully request that it be withdrawn and the claims be allowed.

CONCLUSION

In view of the foregoing, the Applicants believe that Claims 35, 48-52, 54-61, 65, and 72-82 present allowable subject matter and the prompt allowance thereof is requested. If any impediment to the allowance of these claims remains after consideration of the present amendment and above remarks, and such impediment could be removed during a telephone interview, the Examiner is invited to telephone the undersigned attorney, so that such issues may be resolved as expeditiously as possible.

Please charge any additional fees except for Issue Fee or credit any overpayment to Deposit Account No. 20-0100.

Dated this 31st day of October, 2007.

Respectfully submitted,

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